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FULBRIGHT & JAWORSKI, LLP
666 FIFTH AVE
NEW YORK, NY 10103-3198

EXAMINER	
DAVIS, MINH TAM B	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/583,848	Applicant(s) GAUGLER ET AL.	
	Examiner MINH-TAM DAVIS	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-36* is/are pending in the application.

4a) Of the above claim(s) *36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 22-35, drawn to a nucleic acid molecule encoding a tumor rejection antigen precursor, or a fragment thereof, the complement sequence of which hybridizes under stringent conditions to SEQ ID NO:18, or the nucleotide sequence of SEQ ID NO:18, a vector comprising said nucleic acid molecule, and a host cell transfected with said nucleic acid molecule, classified in class 536, subclass 23.1.

II. Claim 36, drawn to a protein encoded by a nucleic acid molecule, the complement sequence of which hybridizes under stringent conditions to SEQ ID NO:18, classified in class 530, subclass 350.

The inventions are distinct, each from each other because of the following reasons:

The products of groups I, II are patentably distinct, because they are drawn to entirely different biochemicals , having different structures.

Because these inventions are distinct for the reason given above and have acquired a separate status in the art, and because the searches for the groups are not co-extensive, restriction for examination purposes as indicated is proper.

Applicants are required under 35 USC 121 to elect a single disclosed group for prosecution on the merits to which the claims shall be restricted.

A telephone call was made to Norman Hanson on 11/21/01 to request an oral election to the above restriction requirement, and resulted in an election with traverse to prosecute the invention of group I, claims 22-35. The traverse is on the ground that

there would not be a serious burden for the Examiner to search the two groups together, and that in one of the parent cases, the two groups were not separated. Applicant further asserts to reserve the right to petition.

The traverse is found not to be persuasive for the following reasons: The products of groups I and II are structurally distinct, and the searches for the two groups are not co-extensive. Therefore, it would be a burden for the Examiner to search and examine the two groups together. Further, the specific parent case number was not recited.

Accordingly, claims 22-35 are examined in this application. Affirmation of this election must be made by applicant in responding to this Office action.

Applicants are reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendement of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. 1.48(b) and by the fee required under 37 C.F.R. 1.17(h).

SEQUENCE RULE COMPLIANCE

Lacey This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. 1.821-25 for the following reasons:

The sequences in the specification, for example on pages 28 and 36, and figure 9 legend, are not accompanied by sequence identification numbers.

PRIORITY DATE

The Examiner has established a priority date 12/12/1991 for the instantly claimed application serial number 09/583848 as the applications 07/764364, 07/728838, 07/705702 to which priority is claimed does not recite SEQ ID NI:18. Applicant is invited to submit evidence pointing to the serial number, page and line where support can be found establishing an earlier priority date.

REJECTION UNDER 35 USC 112, SECOND PARAGRAPH

Claims 22-35 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 22-35 are indefinite because claim 22 is drawn to stringent hybridization conditions. Stringent conditions are not defined by the claim (which reads on the full range of stringent conditions, that is from very permissive to very high stringency). Further, although the specification describes stringent conditions as referred to the conditions described on page 34, second paragraph, the specification also further discloses that said conditions are subject to routine art recognized "modification" (p.34, line 27-28). The specification does not provide a standard for ascertaining the requisite degree of stringent conditions and one of ordinary skill in the art would not be

reasonably apprised of the scope of the invention and would not be able to determine the metes and bounds of the claims.

REJECTION UNDER 35 USC 101, UTILITY

35 U.S.C. 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 22-35 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

Claims 22-35 are drawn to a nucleic acid molecule encoding a tumor rejection antigen precursor (TRAP), or a fragment thereof, the complement sequence of which hybridizes under stringent conditions to SEQ ID NO:18, or the nucleotide sequence of SEQ ID NO:18, a vector comprising said nucleic acid molecule, and a host cell transfected with said nucleic acid molecule.

The specification discloses that SEQ ID NO:18 or MAGE-6 is a cDNA prepared from mRNA of a melanoma cell line (Example 32 on pages 35-36). The specification discloses the contemplation of the use of TRAP as a vaccine against cancer or producing CTLs against cancer cells, generation of antibodies against TRAP for diagnosis and treatment of cancer (p.44-46).

No disclosure, however, is found in the specification whether SEQ ID NO:18 is expressed in tissue, and even if SEQ ID NO:18 is expressed in tissue, whether it is overexpressed in cancer tissue as compared to normal tissues. Further, neither the specification nor any art of record teaches what the polynucleotide is, what it does, does not teach a relationship to any specific disease or establish any involvement of the polypeptide in the etiology of any specific disease or teach which fragments might be active. The asserted utilities for TRAP or MAGE-6, such as production of and screening of antibodies to MAGE-6 apply to many unrelated polypeptide structure sequences. Therefore, the asserted utilities are not considered "specific" utilities, i.e. they are not specific to MAGE-6. Additional disclosed utilities for MAGE-6 include therapy and diagnosis of conditions and diseases characterized by the expression of MAGE-6 . The asserted utilities for MAGE-6 is based on the assertion that MAGE-6 (SEQ ID NO:18) is expressed in a melanoma cell line. One cannot extrapolate expression of SEQ ID NO:18 in melanoma cells in culture to its expression in melanoma cells *in vivo*, because cell culture artifacts are well known in the art and characteristics of cultured cell lines generally differ significantly from the characteristics of a primary tumor. Drexler et al (Leukemia and Lymphoma, 1993, 9:1-25) specifically teach, in the study of Hodgkin and Reed-Sternberg cancer cells in culture, that the acquisition or loss of certain properties during adaptation to culture systems cannot be excluded and that only a few cell lines containing cells that resemble the *in-vivo* cancer cells have been established and even for the *bona fide* cancer cell lines it is difficult to prove that the immortalized cells originated from a specific cancer cell (see attached abstract). Further, Embleton et al

(Immunol Ser, 1984, 23:181-207) specifically teaches that in procedures for the diagnosis of osteogenic sarcoma, caution must be used when interpreting results obtained with monoclonal antibodies that had been raised to cultured cell lines and specifically teach that cultured tumor cells may not be antigenically typical of the tumor cell population from which they were derived and it is well established that new artifactural antigens can occur as a result of culture (see attached abstract). Hsu (in Tissue Culture Methods and Applications, Kruse and Patterson, Eds, 1973, Academic Press, NY, see abstract, p.764) specifically teaches that it is well known that cell cultures *in vitro* frequently change their chromosomal constitutions (see abstract). The evidence presented clearly demonstrates that in cell culture systems, in general, and in cancer derived cell lines in particular, that artifactural chromosome constitutions and antigen expression are expected and must be taken into account when interpreting data received from cell line assays. Further, Freshney (Culture of Animal Cells, A Manual of Basic Technique, Alan R. Liss, Inc., 1983, New York, p4) teach that it is recognized in the art that there are many differences between cultured cells and their counterparts *in vivo*. These differences stem from the dissociation of cells from a three-dimensional geometry and their propagation on a two-dimensional substrate. Specific cell interactions characteristic of histology of the tissue are lost. The culture environment lacks the input of the nervous and endocrine systems involved in homeostatic regulation *in vivo*. Without this control, cellular metabolism may be more constant *in vitro* but may not be truly representative of the tissue from which the cells were derived. This has often led to tissue culture being regarded in a rather skeptical light (p. 4, see Major

Differences *In Vitro*). Further, Dermer (Bio/Technology, 1994, 12:320) teaches that, "petri dish cancer" is a poor representation of malignancy, with characteristics profoundly different from the human disease Further, Dermer teaches that when a normal or malignant body cell adapts to immortal life in culture, it takes an evolutionary - type step that enables the new line to thrive in its artificial environment. This step transforms a cell from one that is stable and differentiated to one that is not, yet normal or malignant cells *in vivo* are not like that. The reference states that evidence of the contradictions between life on the bottom of a lab dish and in the body has been in the scientific literature for more than 30 years. Clearly it is well known in the art that cells in culture exhibit characteristics different from those *in vivo* and cannot duplicate the complex conditions of the *in vivo* environment involved in host-tumor and cell-cell interations. Thus, based on the cell culture data presented in the specification, it could not be predicted that, in the *in vivo* environment, SEQ ID NO:18 is expressed. Further, even if SEQ ID NO:18 is expressed in cancer tissue, one cannot predict whether it is overexpressed in cancer tissue as compared to normal tissue, because it is well known in the art that not any polynucleotide is overexpressed in cancer tissue as compared to normal tissue.

Further, the specification provides no exemplification of or guidance on how to use the claimed vaccine formulation or antigen for active immunotherapy in humans. The goal of tumor vaccination is the induction of tumor immunity to prevent tumor recurrence and to eliminate residual disease. However, Ezzell (J. NIH Res, 1995, 7:46-49) reviews the current thinking in cancer vaccines and states that tumor

immunologists are reluctant to place bets on which cancer vaccine approach will prove effective in the long run (see the entire document, particularly last paragraph) and further states that no one is very optimistic that a single peptide will trigger an immune response strong enough to eradicate tumors or even to prevent the later growth of micrometastases among patients whose tumors have been surgically removed or killed by radiation or chemotherapy (p 48, para 6). In addition, Spitler (Cancer Biotherapy, 1995, 10:1-3) recognizes the lack of predictability of the nature of the art when she states that "Ask practicing oncologists what they think about cancer vaccines and you're likely to get the following response: "cancer vaccines don't work". Ask a venture capitalist or the director of product development at a large pharmaceutical company and you're likely to get the same response." (p 1, para 1). Furthermore, Boon (Adv Can Res, 1992, 58:177-210) teaches that for active immunization in human patients we have to stimulate immune defenses of organisms that have often carried a large tumor burden. Establishment of immune tolerance may therefore have occurred and it may prevent immunization and several lines of evidence suggest that large tumor burdens can tolerize or at least depress the capability to respond against the tumor (p. 206, para 2). In addition, Boon teaches even if activated CTLs are significantly increased, the therapeutic success remains unpredictable due to inconsistencies in antigen expression or presentation by tumor cells (p.178, paragraph before last paragraph).

Thus, none of the utilities identified by Applicant have been demonstrated to be specific to the claimed MAGE-6 (SEQ ID NO:18), and no practical benefit has been shown for the use of the claimed MAGE-6 (SEQ ID NO:18). Given this consideration,

the claimed polynucleotide has no "well-established" use. The artisan is required to perform further experimentation on the claimed material itself in order to determine to what "use" any expression information regarding the claimed polynucleotide could be put.

The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed nucleic acids. Because the claimed invention is not supported by a specific asserted utility for the reasons set forth, credibility of any utility cannot be assessed.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

Keep The instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing.

Claims 22-24, 26-35 are rejected under 35 USC 112, first paragraph.

Claims 22, 24, 26-35 are drawn to a nucleic acid molecule, encoding a tumor rejection antigen precursor, or a fragment thereof, the "complement" sequence of which hybridizes under stringent conditions to SEQ ID NO:18.

Claim 23 is drawn to a "genomic DNA", encoding a tumor rejection antigen precursor, or a fragment thereof, the complement sequence of which hybridizes under stringent conditions to SEQ ID NO:18.

It is noted that a complement could be complete or partial complement, wherein a partial complement could share with SEQ ID NO:18 only a few nucleotides. Thus the claims 22, 24-35 encompass numerous unrelated sequences which share with SEQ ID NO:18 only a few nucleotides.

The specification discloses an isolated cDNA sequence, SEQ ID NO: 18. No disclosure is found in the specification of a structure of a genomic DNA encoding a tumor rejection antigen precursor, or a fragment thereof, the complement sequence of which hybridizes under stringent conditions to SEQ ID NO:18.

The findings of *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412) are clearly relevant to the instant rejection. The court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

The instant specification fails to provide sufficient descriptive information, such as definitive strutural or functional features of the claimed genus of complementary polynucleotides which hybridize under stringent conditions to SEQ ID NO:18. There is

no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description, however, of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides encompassed and no identifying characteristic or property of the instant polynucleotides is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

Further, the specification fails to identify and describe the 5' and 3' regulatory regions and untranslated regions essential to the function of the claimed invention, which are required since the claimed invention currently encompasses the genomic DNA. The art indicates that the structures of genes with naturally occurring regulatory elements and untranslated regions is empirically determined (Harris et al. J. of The Am Society of Nephrology 6:1125-33, 1995; Ahn et al. Nature Genetics 3(4):283-91, 1993; and Cawthon et al. Genomics 9(3):446-60, 1991). Therefore, the structure of these elements is not conventional in the art and skilled in the art would therefore not recognize from the disclosure that applicant was in possession of the genomic DNA, or a fragment thereof, the complement sequence of which hybridizes under stringent conditions to SEQ ID NO:18.

Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of a specific nucleotide sequence, is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Thus, only an isolated cDNA molecule comprising SEQ ID NO: 18, but not the full breadth of the claims meet the written description provisions of 35 USC 112, first paragraph.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT

Keep

Claims 22-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Specifically, since the claimed invention is not supported by a well established utility for the reasons set forth in the rejection under 35 USC 101 above, one skilled in the art clearly would not know how to make/use the claimed invention.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE

Keep

1. If Applicant could overcome the above 101 and 112, first paragraph rejections, claims 22-24, 26-35 are still rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:18, does not reasonably provide

enablement for a nucleic acid molecule, the "complement" sequence of which "hybridizes under stringent conditions" to SEQ ID NO:18. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 22-24, 26-35 are drawn to a nucleic acid molecule encoding a tumor rejection antigen precursor, or a fragment thereof, the "complement" sequence of which "hybridizes under stringent conditions" to SEQ ID NO:18, a vector comprising said nucleic acid molecule, and a host cell transfected with said nucleic acid molecule.

It is noted that a complement could be complete or partial complement, wherein a partial complement could share with SEQ ID NO:18 only a few nucleotides. Thus the claims 22-24, 26-35 encompass numerous unrelated sequences which share with SEQ ID NO:18 only a few nucleotides.

It is further noted that "hybridizes under stringent conditions" encompasses hybridization under a range of stringent conditions, from very low stringency to high stringency. It is well known in the art that under very low stringency conditions, unrelated sequences with low sequence similarity would hybridize to SEQ ID NO:18.

Claims 22-24, 26-35 encompass non-disclosed nucleic acid sequences attached to SEQ ID NO: 18. That is a nucleic acid molecule encoding a tumor rejection antigen precursor, or a fragment thereof, the complement sequence of which hybridizes under stringent conditions to SEQ ID NO:18. When given the broadest reasonable interpretation, the claims are clearly intended to encompass unrelated full-length cDNAs, genes and protein coding regions. Clearly, it would be expected that a

substantial number of the hybridizing or complementary polynucleotides encompassed by the claims **would not** share either structural or functional properties with the polynucleotide of SEQ ID NO: 18. For the above reasons, undue experimentation would be required to practice the claimed invention.

Keep

2. If Applicant could overcome the above 101 and 112, first paragraph rejections, claims 22-35 are still rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:18, does not reasonably provide enablement for a nucleic acid molecule "encoding" a tumor rejection antigen precursor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 22-35, are drawn to a nucleic acid molecule "encoding" a tumor rejection antigen precursor, or a fragment thereof, the complement sequence of which hybridizes under stringent conditions to SEQ ID NO:18, or the nucleotide sequence of SEQ ID NO:18, a vector comprising said nucleic acid molecule, and a host cell transfected with said nucleic acid molecule.

The specification discloses that SEQ ID NO:18 or MAGE-6 is a cDNA prepared from mRNA of a melanoma cell line (Example 32 on pages 35-36). No disclosure is found in the specifition concerning a detection of a tumor rejection precursor encoded by SEQ ID NO:18 in any tissue.

The claims however encompass a nucleic acid molecule which is translated into a protein in tissue *in vivo*.

It is well known in the art that regulation of mRNA translation is one of the major regulatory steps in the control of gene expression (Jansen, M et al, 1995, Pediatric Res, 37 (6): 681-686). Further, those of skill in the art recognize that expression of mRNA, specific for a tissue type, does not dictate nor predict the translation of such mRNA into a polypeptide. For example, Alberts et al. (Molecular Biology of the Cell, 3rd edition, 1994, page 465) teach that translation of ferritin mRNA into ferritin polypeptide is blocked during periods of iron starvation. Likewise, if excess iron is available, the transferrin receptor mRNA is degraded and no transferrin receptor polypeptide is translated. Many other proteins are regulated at the translational level rather than the transcriptional level. For instance, Shantz and Pegg (Int J of Biochem and Cell Biol., 1999, Vol. 31, pp. 107-122) teach that ornithine decarboxylase is highly regulated in the cell at the level of translation and that translation of ornithine decarboxylase mRNA is dependent on the secondary structure of the mRNA and the availability of eIF-4E, which mediates translation initiation. McClean and Hill (Eur J of Cancer, 1993, vol. 29A, pp. 2243-2248) teach that p-glycoprotein can be overexpressed in CHO cells following exposure to radiation, without any concomitant overexpression of the p-glycoprotein mRNA. In addition, Fu et al (EMBO Journal, 1996, Vol. 15, pp. 4392-4401) teach that levels of p53 protein expression do not correlate with levels of p53 mRNA levels in blast cells taken from patients with acute myelogenous leukemia, said patients being without mutations in the p53 gene. Yokota, J et al (Oncogene, 1988,Vol.3, pp. 471-475) teach that the retinoblasma (RB) 115 kD protein is not detected in all nine cases of lung small-cell carcinoma, with either normal or abnormal size mRNA, whereas the RB protein is

detected in three of four adenocarcinomas and all three squamous cell carcinomas and one of two large cell carcinomas expressing normal size RB mRNA. Thus, predictability of protein translation or the extent of translation is not solely contingent on mRNA expression due to the multitude of homeostatic factors affecting transcription and translation. For the above reasons, one of skill in the art would not be able to predict if SEQ ID NO:18 is translated into a polypeptide expression product, or even if translated, whether it is overexpressed. In view of the above, one of skill in he art would be forced into undue experimentation to practice the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 22 is rejected under 35 U.S.C. 102(b) as being anticipated by Kudo et al, US PN=4,786,719.

Claim 22 is drawn to a fragment of a nucleic acid molecule encoding a tumor rejection antigen precursor (TRAP), the complement sequence of which hybridizes under stringent conditions to SEQ ID NO:18

Kudo et al teach a DNA sequence (the first sequence listed on the first page of the patent), the fragment TGCAGCTGGT of which is 100% similar to a fragment of SEQ ID NO:18 from nucleotide 41 to 50.

Given the polynucleotide sequence taught by Kudo et al, one of ordinary skill in the art would immediately envision the claimed fragment.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

MINH TAM DAVIS

May 24, 2002

SUSAN UNGAR, PH.D
PRIMARY EXAMINER